

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
13 May 2004 (13.05.2004)

PCT

(10) International Publication Number  
**WO 2004/039308 A3**

- (51) International Patent Classification<sup>7</sup>: **A61K 31/517**
- (21) International Application Number: **PCT/IL2003/000900**
- (22) International Filing Date: 30 October 2003 (30.10.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/422,487 31 October 2002 (31.10.2002) US
- (71) Applicants (*for all designated States except US*): **STATE OF ISRAEL, MINISTRY OF AGRICULTURE [IL/IL]**; Agricultural Research Organization, Volcani Center, P.O. Box 6, 50250 Bet Dagan (IL). **HADASIT MEDICAL RESEARCH SERVICES AND DEVELOPMENT LTD. [IL/IL]**; P.O. Box 12000, 91120 Jerusalem (IL). **COLL-GARD BIOPHARMACEUTICALS LTD. [IL/IL]**; 1B Bazel Street, Kiryat Arie, 49170 Petach Tikva (IL).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **PINES, Mark [IL/IL]**; 8 Hasigaliot Street, Havazelet, 76605 Rehovot (IL). **NAGLER, Arnon [IL/IL]**; 46 Sderot Herzl, 74381 Jerusalem (IL). **YARKONI, Shai [IL/IL]**; 33 Lamed Hey Street, 44395 Kfar Saba (IL).
- (74) Agent: **WEBB, Cynthia**; Webb & Associates, P.O. Box 2189, 76121 Rehovot (IL).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— *with international search report*  
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*
- (88) Date of publication of the international search report:  
8 July 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: QUINAZOLINONE COMPOSITIONS FOR REGULATION OF GENE EXPRESSION RELATED TO PATHOLOGICAL PROCESSES

(57) Abstract: The present invention relates to pharmaceutical compositions for modifying gene expression in a pathological process, thereby preventing or ameliorating said process. More particularly the compositions comprise quinazolinones, especially halofuginone, for inhibiting or preventing alterations in gene expression during fibrosis. The present invention particularly relates to pharmaceutical compositions for improving the regeneration of cirrhotic liver.

WO 2004/039308 A3

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL03/00900

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 31/517

US CL : 514/266.22, 266.21, 266.2

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/266.22, 266.21, 266.2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONEElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,277,989 A (CHAKRAVARTY et al.) 21 August 2001, see abstract and entire document.	1-26
Y	US 6,028,075 A (PINE et al.) 22 February 2000, see abstract and columns 1-8.	1-26
Y,P	US 6,562,829 B1 (PINES et al.) 13 May 2003, see abstract and columns 1-10.	1-26

☐

Further documents are listed in the continuation of Box C.

☐

See patent family annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

03 February 2004 (03.02.2004)

Date of mailing of the international search report

27 MAY 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (703) 305-3230

Authorized officer

Edwayne C. Jones

Telephone No. (571) 272-1600

# INTERNATIONAL SEARCH REPORT

PCT/IL03/00900

## Continuation of B. FIELDS SEARCHED Item 3:

WEST, PGPUB, USPTO, USOC, EPAB, JPAB, DWPI search terms include: cirrho\$6, quinazolinone or quinazolinon\$6, liver, (gene near5 regulat\$8), expression or express